

EXHIBIT C
MARKED VERSION OF THE CLAIMS
AMENDMENT (Filed *DRAFT*)

**U.S. PATENT APPLICATION SERIAL NO. TO BE ASSIGNED, DIVISIONAL OF
U.S. PATENT APPLICATION SERIAL NO. 09/222,596**

14. (Amended) A method for determining a probability that an expression level of a cellular constituent in a plurality of paired differential microarray experiments is altered by a perturbation, wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments comprises a first microarray experiment representing a baseline state of a first biological system, and a second microarray experiment representing a perturbed state of said first biological system, said method comprising the steps of

(a) determining an error distribution statistic by fitting a reference pair of microarray experiments with an intensity independent statistic, wherein said reference pair of microarray experiments comprises a first reference microarray experiment, and a second reference microarray experiment that is a nominal repeat of said first reference microarray experiment;

(b) [selecting said cellular constituent from a set of cellular constituents measured in said plurality of paired differential microarray experiments, and, for each paired differential microarray experiment in said plurality of paired differential microarray experiments,]
determining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, an amount of change in expression level of said cellular constituent between the second microarray experiment and the first microarray experiment of said paired differential microarray experiment using said error distribution statistic; and

(c) determining said probability that said expression level of said cellular constituent in said plurality of paired differential microarray experiments is altered by said perturbation by combining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, [said] each amount of change in expression level of said cellular constituent determined in step (b) [for each paired differential microarray experiment in said plurality of paired differential microarray experiments] using a rank based method.

15. (Amended) A computer system for determining a probability that an expression level of a cellular constituent in a plurality of paired differential microarray experiments is altered by a perturbation, wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments comprises a first microarray experiment representing a baseline state of a first biological system, and a second microarray experiment representing a perturbed state of said first biological system; the computer system comprising a processor, and a memory encoding one or more programs coupled to the processor and the one or more programs cause the processor to perform a method comprising the steps of

(a) determining an error distribution statistic by fitting a reference pair of microarray experiments with an intensity independent statistic, wherein said reference pair of microarray experiments comprises a first reference microarray experiment, and a second reference microarray experiment that is a nominal repeat of said first reference microarray experiment;

(b) [selecting said cellular constituent from a set of cellular constituents measured in said plurality of paired differential microarray experiments, and, for each paired differential microarray experiment in said plurality of paired differential microarray experiments,] determining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, an amount of change in expression level of said cellular constituent between the second microarray experiment and the first microarray experiment [of said paired differential microarray experiment] using said error distribution statistic; and

(c) determining said probability that said expression level of said cellular constituent in said plurality of paired differential microarray experiments is altered by said perturbation by combining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, [said] each amount of change in expression level of said cellular constituent determined in step (b) [for each paired differential microarray experiment in said plurality of paired differential microarray experiments] using a rank based method.

16. (Amended) The method of Claim 14 wherein said error distribution statistic is calculated according to a formula

$$\frac{(X - Y)}{\sqrt{\sigma_X^2 + \sigma_Y^2 + f^2(X^2 + Y^2)}}$$

where X represents an intensity of said [a] cellular constituent in said first microarray experiment of said reference pair of microarray experiments, Y represents an intensity of said cellular constituent in said second microarray experiment of said reference pair of microarray experiments, σ_X^2 is a variance term for X that represents an additive error level in X, σ_Y^2 is a variance term for Y that represents an additive error level in Y, and f is a fractional multiplicative error level.

17. (Amended) The computer system of Claim 15 wherein said error distribution statistic is calculated according to a formula

$$\frac{(X - Y)}{\sqrt{\sigma_X^2 + \sigma_Y^2 + f^2(X^2 + Y^2)}}$$

where X represents an intensity of said [a] cellular constituent in said first microarray experiment of said reference pair of microarray experiments, Y represents an intensity of said cellular constituent in said second microarray experiment of said reference pair of microarray experiments, σ_X^2 is a variance term for X that represents an additive error level in X, σ_Y^2 is a variance term for Y that represents an additive error level in Y, and f is a fractional multiplicative error level.

18. (Amended) The method of Claim 16 wherein said rank based method comprises determining a rank for said amount of change in expression level of said cellular constituent between said second microarray experiment and said first microarray experiment of said paired differential microarray experiment in relation to all cellular constituent [contituents] measurements in said plurality of paired differential microarray experiments using said error distribution statistic [according to a magnitude derived by the formula of Claim 16].

19. (Amended) The computer system of Claim 17 wherein said rank based method comprises determining a rank for said amount of change in expression level of said cellular constituent between said second microarray experiment and said first microarray experiment of said paired differential microarray experiment in relation to all cellular constituent [contituents]

measurements in said plurality of paired differential microarray experiments using said error distribution statistic [according to a magnitude derived by the formula of Claim 17].

20. (Amended) The method of Claim 14 wherein said rank based method determines a probability that said [a] cellular constituent is up-regulated in response to a perturbation.

21. (Amended) The computer system of Claim 15 wherein said rank based method determines a probability that said [a] cellular constituent is up-regulated in response to a perturbation.

22. (Amended) The method of Claim [20] 14 wherein said rank based method comprises computing [has the form]

$$P(H_0^+) = \prod_i P_i$$

where P_i is the percentile rank of the expression of said cellular constituent in the i^{th} pair [said probability that a cellular constituent is up-regulated in said plurality] of paired differential microarray experiments in said plurality of paired differential microarray experiments [experiment i , i is a paired differential microarray experiment selected from said plurality of paired differential microarray experiments, P is said probability that said expression level of said cellular constituent is up-regulated in response to said perturbation] , and $P(H_0^+)$ is the chance that said cellular constituent is not up-regulated in said plurality of paired differential microarray experiments.

23. (Amended) The method of Claim 14 wherein said rank based method determines a probability that said [a] cellular constituent is down-regulated in response to [a] said perturbation.

24. (Amended) The method of Claim [23] 14 wherein said rank based method comprises computing [has the form]

$$P(H_0^-) = \prod_i (1 - P_i)$$

where P_i is the percentile rank of the expression of said cellular constituent in the i^{th} pair [said probability that a cellular constituent is down-regulated in] of paired differential microarray experiments in said plurality of paired differential microarray experiments [experiment i , is selected from said plurality of paired differential microarray experiments, and P is said probability that said cellular constituent is down-regulated in response to said perturbation] , and $P(H_0)$ is the chance that said cellular constituent is not up-regulated in said plurality of paired differential microarray experiments.

25. (Amended) The method of Claim 14 wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments is a two-fluorophore microarray experiment [experiments] wherein a first fluorophore represents said baseline state of said biological system and a second fluorophore, distinguishable from said first fluorophore, represents said perturbed state of said biological system.

26. (Amended) The method of Claim 14 wherein a single fluorophore is used in each said paired differential microarray experiments in said plurality of paired differential microarray experiments.

27. (Amended) The method of Claim 14 wherein a first fluorophore [label] is used in said first reference microarray experiment and a second fluorophore, distinguishable from said first fluorophore, [label] is used in said second reference microarray experiment.